

### REMARKS

Claims 18-31 are pending in the above-identified application. All claims stand rejected under 35 U.S.C. § 103(a) for obviousness over Constantz et al. (U.S. Patent No. 5,820,632; hereinafter “Constantz”) in view of Niwa et al. (U.S. Patent No. 4,429,691; hereinafter “Niwa”) and Sugihara et al. (WO 90/00892; hereinafter “Sugihara”), and further in view of Spampata et al. (J. Oral Maxillofac. Surg. 50:140-151, 1992; hereinafter “Spampata”), and Glowacki et al. (U.S. Patent No. 4,440,750; hereinafter “Glowacki”). Applicants address the Examiner’s rejection below.

#### Amendment to the Drawings

As requested by the Examiner, Applicants submit a replacement drawing sheet for Figures 4A and 4B (corresponding to sheet 3/19), which clearly identifies Figure 4B, and a replacement drawing sheet for Figures 16A and 16B (corresponding to sheet 14/19), which clearly identifies Figure 16A and Figure 16B. No new matter is added by the amendment.

#### Rejection under 35 U.S.C. § 103(a)

The Examiner rejects claims 18-31 under 35 U.S.C. § 103(a) for obviousness over Constantz in view of Niwa and Sugihara, and further in view of Spampata and Glowacki. The Examiner states:

Although...there is no demineralized bone specified in the primary reference, the prior art, sampata [sic] shows it is well known and old, and here utilized shows it to favor induction of osteogenic activity when implanted.

Therefore, inclusion of this demineralized bone powder with the materials

cited by constants [sic], inclusive of osteogenic factors...would be an obvious element to enhance bone repair. (Office Action, p. 2.)

Applicants respectfully traverse this rejection.

The Legal Standard for Obviousness under 35 U.S.C. § 103

To establish a *prima facie* case of obviousness under § 103, the Examiner must demonstrate that the differences between the claimed invention and the prior art are such that the subject matter as a whole would have been obvious, at the time the invention was made, to a person having ordinary skill in the art. See 35 U.S.C. § 103(a) (Supp. III 1997); *In re Dembiczak*, 175 F.3d 994, 998, 50 USPQ2d 1614, 1616 (Fed. Cir. 1999). Whether or not a claimed invention is obvious is a legal conclusion based on underlying factual inquiries, including: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) objective evidence of nonobviousness. *Id.*

Importantly, where “claimed subject matter has been rejected as obvious in view of a combination of references, a proper analysis under § 103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should . . . carry out the claimed process; and (2) whether the prior art would have revealed that in so . . . carrying out, those of ordinary skill would have a reasonable expectation of success.” *In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). Furthermore, “[b]oth the suggestion and the expectation of success must be founded in the prior art, not in the applicant’s disclosure.” *In re Dow Chem. Co.*, 837 F.2d 469, 473, 5 USPQ2d

1529, 1531 (Fed. Cir. 1988). As the Federal Circuit recently observed:

A critical step in analyzing the patentability of claims pursuant to section 103(a) is casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field. . . . Most if not all inventions arise from a combination of old elements. . . . Thus, every element of a claimed invention may often be found in the prior art. . . . However, identification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention. . . . Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, *there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant.*

*In re Kotzab*, 217 F.3d 1365, 1369-70, 55 USPQ2d 1313, 1316 (Fed. Cir. 2000)(emphasis added)(citations omitted). The evidence of a suggestion, teaching, or motivation to combine “must be clear and particular.” *Dembiczak*, 175 F.3d at 999. “Defining the problem in terms of its solution reveals improper hindsight in the selection of the prior art relevant to obviousness.” *Monarch Knitting Mach. Corp. v. Sulzer Morat GmbH*, 139 F.3d 877, 880, 45 USPQ2d 1977, 1981 (Fed. Cir. 1998). “Broad conclusory statements regarding the teaching of multiple references, standing alone, are not ‘evidence.’” *Id.*

Thus, the case law clearly mandates that, even if the Examiner identifies every element of a claimed invention in various pieces of the prior art, this alone is insufficient to negate patentability. Otherwise, “rejecting patents solely by finding prior art corollaries for the claimed elements would permit an examiner to use the claimed invention as a blueprint for piecing together elements in the prior art to defeat the patentability of the claimed invention.” *In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457 (Fed. Cir. 1998). To avoid hindsight based on the invention to defeat patentability of the invention, the Federal Circuit requires an

Examiner to show a motivation to combine the references that create the case of obviousness. *Id.*

That is, “the examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.” *Id.*; emphasis added.

The Federal Circuit has repeatedly emphasized that no invention is obvious under 35 U.S.C. § 103(a) simply because it would have been “obvious to try.” *See Gillette Co. v. S.C. Johnson & Son, Inc.*, 919 F.2d 720, 725, 16 USPQ2d 1923, 1928 (Fed. Cir. 1990); *In re O’Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988); *Dow*, 837 F.2d at 473, 5 USPQ2d at 1532; *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1380 231 USPQ 81, 90-91 (Fed. Cir. 1986); *Jones v. Hardy*, 727 F.2d 1524, 1530, 220 USPQ 1021, 1026 (Fed. Cir. 1984).

An “obvious to try” situation exists when a general disclosure may pique the scientist’s curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued.

*In re Eli Lilly & Co.*, 902 F.2d 943, 945, 14 USPQ2d 1741, 1743 (Fed. Cir. 1990) (emphases added). Thus, where the prior art gives only general guidance as to the particular form of the claimed invention, or how to achieve it, a *prima facie* case of obviousness has not been established. *Dow*, 837 F.2d at 473, 5 USPQ2d at 1532.

Present Claims 18-31 are Not Obvious Over Constantz, Niwa, Sugihara, Spampata, and Glowacki

In making the present rejection of claims 18-31, the Examiner has merely identified each element of the claims in the cited references; he has not shown, or even argued, that the cited references, in combination, teach, suggest, or motivate the skilled artisan to combine the references to produce the invention of claims 18-31.

Applicants first discuss the deficiencies of Constantz, Niwa, and Sugihara.

Constantz, Niwa, and Sugihara, Alone and in Combination, Fail to Teach or Suggest an Implant Composition Comprising Demineralized Bone Matrix

Claims 18-31 are directed to a self-hardening implant composition comprising a calcium phosphate in combination with demineralized bone matrix. Constantz discloses a calcium phosphate cement composition, e.g., hydroxyapatite, capable of setting to form a bone-like material (see, e.g., col. 2, lines 28-43). The Constantz composition is formed by combining a calcium source, a phosphoric acid source, and a lubricant (e.g., a water, gel, or colloid; see, e.g., col. 3, lines 3-17). Constantz states:

In many situations, a wide variety of additives may be included in the medium to provide for specific properties. One group of additives is protein. Bone associated proteins may be added to modify the physical properties of the composition, enhance resorption, angiogenesis, cell entry and proliferation, mineralization, bone formation, growth of osteoclasts and/or osteoblasts, or the like. Proteins of particular interest are the different types of collagen, particularly Type I. Other proteins include osteonectin, bone sialoproteins (Bsp), alpha-2HS-glycoproteins, bone Gla-protein (Bgp), matrix Gla-protein, bone phosphoglycoprotein, bone phosphoprotein, bone proteoglycan, protolipids, bone morphogenic protein, cartilage induction factor, platelet derived growth factor and skeletal growth factor. Other proteins associated with other parts of human or other mammalian anatomy, include proteins associated with cartilage, such as

chondrocalcinizing protein; proteins associated with dentin, such as phosphophoryn, glycoproteins and Gla proteins; or proteins associated with enamel, such as amelogenin and enamelin. (col. 6, lines 23-42).

As is evident from the cited passage, Constantz discloses that the cement composition may optionally include a bone-associated protein additive. Constantz does not teach or suggest that the additive can be anything other than a bone associated protein or that the protein can be provided in a substantially impure form. Constantz certainly fails to teach or suggest that additive can be demineralized bone matrix, which is a complex composition containing approximately 99% matrix components (i.e., non-protein components) and only about 1% protein components; the components, many of which are unknown, being provided in a substantially impure form. By limiting the disclosure of additives to proteins, Constantz fails to teach or suggest that the additive could be demineralized bone matrix, a substantially impure, heterogeneous composition that consists of primarily non-proteinaceous components. Therefore, Constantz not only fails to teach or suggest the use of demineralized bone matrix, Constantz also fails to guide the skilled artisan to look beyond the Constantz disclosure to identify additives other than proteins for use in Constantz' cement composition.

Niwa also fails to disclose the combination of a calcium phosphate with demineralized bone matrix. Niwa merely discloses an apatitic calcium phosphate composition for filling in defects or hollow portions of bones, which may be mixed with "cancellous bone obtained by crushing a bone" (see col. 7, lines 6-10). Crushed cancellous bone is not equivalent to demineralized bone matrix because it is prepared by simply crushing the bone, while demineralized bone matrix is prepared in a multi-step process that includes crushing and grinding the bone to form a powder, defatting and dehydrating the crushed bone powder, exposing the

defatted and dehydrated crushed bone powder to acid, and finally, rinsing the acid away and dehydrating the resultant product (see, e.g., Spampata, p. 141). Clearly, Niwa does not teach or suggest the preparation of demineralized bone matrix. Therefore, Niwa, in combination with Constantz, fails to teach or suggest the combination of demineralized bone matrix with a calcium phosphate to form the implant composition of present claims 18-31.

Sugihara also fails to teach or suggest an implant composition comprising a calcium phosphate in combination with demineralized bone matrix. Sugihara merely discloses “hardening materials for medical and dental service...composed of a calcium phosphate powder and a hardening liquid and also...collagen and/or collagen derivatives” (see, e.g., page 2, lines 20-24). Sugihara does not teach or suggest that demineralized bone matrix can be combined with the calcium phosphate powder or that demineralized bone matrix can be used as a source of the collagen for use in the Sugihara composition. Therefore, Sugihara cannot be relied upon for a teaching or suggestion to combine a calcium phosphate with demineralized bone matrix, as is recited in present claims 18-31, and fails to remedy the deficiencies of Constantz and Niwa.

Clearly, Constantz, Niwa, and Sugihara, either alone or in combination, fail to teach or suggest a composition containing demineralized bone matrix and a calcium phosphate carrier. Not only do these references lack the necessary teaching or suggestion to motivate the skilled artisan to prepare the implant composition of present claims 18-31, they also fail to motivate the skilled artisan to look beyond their reference teachings to identify other additives, such as demineralized bone matrix, for use in their respective compositions. Therefore, the skilled artisan would not look to Spampata and Glowacki to supplement the Constantz, Niwa, and Sugihara disclosures.

Spampata and Glowacki Fail to Motivate the Skilled Artisan to Combine their Reference

Teachings with those of Constantz, Niwa, or Sugihara

As is discussed above, Constantz, Niwa, and Sugihara disclose calcium phosphate compositions containing bone protein, crushed bone, and collagen or collagen derivatives, respectively. In combination, Constantz, Niwa, and Sugihara do not disclose an implant composition containing a calcium phosphate and demineralized bone matrix. To cure this deficiency, the Examiner now combines Spampata and Glowacki, which describe demineralized bone matrix compositions, with Constantz, Niwa, and Sugihara, arguing that because demineralized bone matrix was known in the art prior to Applicants' filing date, and because Spampata and Glowacki demonstrate the osteogenic activity of demineralized bone matrix, the skilled artisan would be motivated to combine the Spampata and Glowacki compositions with the Constantz composition to yield the implant composition of present claims 18-31. Applicants respectfully disagree.

The M.P.E.P. § 2143.01 states:

The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990).

Furthermore:

A statement that modifications of the prior art to meet the claimed invention would have been “‘well within the ordinary skill of the art at the time the claimed invention was made’” because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references. *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). See also *In re Kotzab*, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1318 (Fed. Cir. 2000).



Spampata describes the osteoinductive activity of demineralized bone powder (DBP), the guanidine-extractable protein fraction of demineralized bone powder (GE), which lacks bone matrix particles, and the insoluble residue of the GE fraction (GR). Glowacki describes the use of a composition containing particulate demineralized bone and reconstituted collagen fibers for repairing bone (see, e.g., col. 1, lines 51-59). Neither Spampata nor Glowacki teaches or suggests the addition of a calcium phosphate component to the demineralized bone containing compositions. Moreover, Spampata and Glowacki do not even teach or suggest the desirability of such a combination. Therefore, the skilled artisan would not be motivated, based solely on the teachings of Spampata or Glowacki, to modify the Spampata or Glowacki compositions to include a calcium phosphate component, or to combine the disclosures of Spampata and Glowacki with Constantz, Niwa, and Sugihara to yield the implant composition of present claims 18-31.

Clearly, the suggestion or motivation to combine Constantz, Niwa, and Sugihara with Spampata and Glowacki cannot be found in the cited references themselves. Therefore, it appears that the Examiner has merely identified each feature of present claims 18-31 in the cited prior art references, arguing that it would be obvious to combine these references to yield the presently claimed implant composition. As is discussed above, this is clearly impermissible where the references do not provide an objective reason to combine reference teachings (see, e.g., M.P.E.P. § 2143.01, *supra*). Furthermore, because the cited references fail to provide the necessary motivation to combine reference teachings, it is improper for the Examiner to rely on the skill of the artisan as a basis for a *prima facie* case of obviousness (see, e.g., M.P.E.P. §

2143.01, *supra*). For all of the reasons provided above, Applicants respectfully request that the rejection of claims 18-31 under 35 U.S.C. § 103(a) over Constantz, Niwa, Sugihara, Spampata, and Glowacki should be withdrawn.

The Suggestion to Combine and Expectation of Success is Found Solely in Applicants'

Disclosure

To establish a *prima facie* case of obviousness under 35 U.S.C. § 103, the prior art must suggest the claimed combination and provide a reasonable expectation of success; these elements cannot be found solely in Applicants' disclosure (see *In re Vaeck, supra*, and *In re Dow Chem. Co., supra*). As is discussed above, Constantz, Niwa, and Sugihara fail to teach or suggest combining a calcium phosphate with demineralized bone matrix, and Spampata and Glowacki fail to remedy this deficiency. The Examiner has not provided a clear motivation from the references to combine the reference teachings prior to the disclosure of Applicant's present invention, nor any expectation of success other than the teachings of Applicants' disclosure. Therefore, both the motivation to combine the cited references and the reasonable expectation of success must be derived solely from the teachings of Applicants' disclosure.

Use of Applicant's disclosure to provide a motivation for combining these references is an improper use of hindsight and cannot be used to establish obviousness. The Federal Circuit has repeatedly cautioned against the "insidious effects of hindsight" in making obviousness determinations. *Life Technologies, Inc. v. Clontech Labs, Inc.*, 224 F.3d 1320, 1326 (Fed. Cir. 2000). More specifically, the court has stated that (*Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 227 U.S.P.Q. 543 (Fed. Cir. 1985)):

it is impermissible to first ascertain factually what [Applicants] did and then view the prior art in such a manner as to select from the random facts of art only those which may be modified and then utilized to reconstruct appellants invention from such prior art.

To avoid the use of hindsight, the M.P.E.P. has adopted the same view, stating that “the mere fact that references can be combined or modified is not sufficient to establish *prima facie* obviousness,” and that the art must provide “an objective reason to combine the teachings.”

M.P.E.P. § 2143.01, *supra*. Further, a generally high level of skill in the art cannot be relied upon to provide such a reason. *Al-Site Corp. v. VSI Int’l Inc.*, 174 F.3d 1308 (Fed. Cir. 1999).

Thus, absent a specific motivation to combine references, a *prima facie* case of obviousness cannot be made.

Because the prior art does not teach, suggest, or motivate the skilled artisan to prepare the composition of present claims 18-31, and because the cited references fail to provide a reasonable expectation of success for making or using such a composition, Applicants respectfully request that the rejection of claims 18-31 under 35 U.S.C. § 103(a) over Constantz, Niwa, Sugihara, Spampata, and Glowacki should be withdrawn.

CONCLUSION

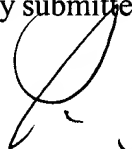
In view of the above remarks, Applicants respectfully submit that the claims are in condition for allowance, and such action is respectfully requested.

Enclosed is a petition to extend the period for replying for two months, to and including June 26, 2004, and a check for the fee required under 37 C.F.R. § 1.17(a).

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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